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PATENT 2900

S/N 10/028,547

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Jay D. Kranzler et al. Examiner: Rebecca Cook  
Serial No.: 10/028,547 Group Art Unit: 1614  
Filed: December 19, 2001 Docket: 1666.003US1  
Title: METHODS OF TREATING FIBROMYALGIA, CHRONIC FATIGUE  
SYNDROME AND PAIN

15/declarations  
1.131

**DECLARATION UNDER 37 CFR § 1.131**

Commissioner for Patents  
Washington, D.C. 20231

I, Jay D. Kranzler, declare and say as follows:

1. I am a co-inventor of the subject matter claimed in the above-identified U.S. Patent Application Serial No. 10/028,547, filed December 19, 2001.
2. I have reviewed the Office Action mailed August 27, 2002, with respect to the above-identified application, and have reviewed Horrobin et al. (WO 01/26623, published April 19, 2001) and Nagaoka et al., ("Beneficial Effects of a Serotonin-noradrenaline . . .", *Medicine and Drug Journal* 37(10):238-240, October 1, 2001), which were cited by the Examiner in the Office Action. I make this Declaration in support of the patentability of the claims of Application Serial No. 10/028,547.
3. Prior to April 19, 2001, the subject matter claimed in the above-identified application was invented in the United States.
4. Evidence that the invention was conceived or reduced to practice before April 19, 2001, can be found in the copy of selected pages of a presentation given to Pierre Fabre (dates and confidential information redacted) attached hereto as Exhibit A. The material was presented by myself, Srinivas Rao, and Wendy Johnson (page 2) to representatives of Pierre Fabre before April 19, 2001. Page 3 discloses that the presentation concerns an agent to treat fibromyalgia syndrome. Pages 31-32 disclose the use of milnacipran to treat fibromyalgia syndrome. Page 34 discloses the idea of trials of milnacipran to treat fibromyalgia syndrome. Thus, the presentation

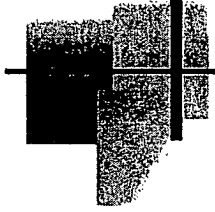
evidences conception or reduction to practice of the subject matter of the claimed invention before April 19, 2001.

5. I further declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

12/3/02  
Date

  
Jay D. Kranzler

## **Appendix A**



# Cypress Bioscience, Inc.

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Pierre Fabre

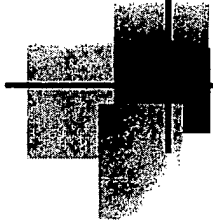
[REDACTED]



# Cypress Attendees

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- Jay Kranzler, MD, PhD  
Chairman and CEO
- Wendy Johnson  
Acting VP of Business Development
- Srinivas Rao, MD, PhD  
Director of Science & Technology



# Today's Agenda

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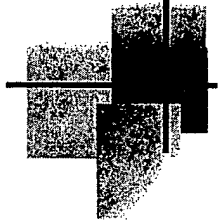
- **Overview of Cypress and Fibromyalgia Syndrome (FMS)**
- Agent Discussion
- Potential Deal Structure
- Next steps



# Milnacipran: Rationale

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- Approaches “ideal” pharmacologic profile
  - Increases both 5-HT and NA tone, likely reducing central sensitization.
  - High specificity may result in improved side-effect profile compared to TCA’s.
- Extensive safety-data in man allows us to move quickly to test our hypotheses

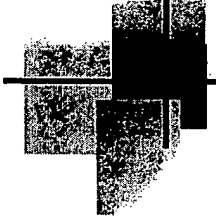


# Information we seek: Pharmacology

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- How does milnacipran compare to:
  - Venlafaxine
  - Duloxetine





# Information we seek: Antidepressant Indication

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- Milnacipram in the marketplace
  - Ranking in European market
  - Yearly sales figures
  - Target patient population
  - Competitive advantages
  - Other indications?

# Information we seek:

## Analgesic Efficacy


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- Animal pain-model data
  - Acute vs. chronic vs. visceral pain
- Trials of milnacipran in FMS or chronic fatigue syndrome?
- Human data for chronic pain

[REDACTED]

[REDACTED]

[REDACTED]



# Today's Agenda

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- Overview of Cypress and Fibromyalgia Syndrome (FMS)
- Milnacipran Discussion
- Potential Deal Structure
- **Next Steps**

# Next Steps

## ■ Step 1: Pierre Fabre

- Determine interest in out-licensing to Cypress
- Provide samples for testing
- Respond to financial proposal

## ■ Step 2: Cypress

- Develop due diligence list, initiate process and complete

[REDACTED]